c. hybridizing the PCR products with probes specific for either the target gene or any adjacent DNA sequences,

d. detecting the presence of rearrangements of the target gene, and, if any rearrangement is detected, identifying the DNA sequences involved.--

REMARKS

Reconsideration is requested.

The claims have been further amended in response to the Examiner's comments in the Advisory Action dated February 14, 2002 (Paper No. 11). Specifically, claim 39 now recites one pair of primers, and claim 25 has been amended to delete the references to 5' and 3' and the phrase "the same on each cycle". The Examiner's comment regarding the phrase "anchored primers" is not understood as the term anchored PCR, to which this refers, is clearly described in the specification and was previously considered by the Examiner with regard to the previously recited "anchored PCR", which the Examiner found indefinite. The amendment to the recited "anchored primers" therefore should not require further search and/or consideration.

Claim 16 has been canceled, without prejudice. Claim 39 has been added, based on canceled claim 16. No new matter has been added. The amendments do not raise new issues requiring further search and/or consideration. The amendments do not add new claims without canceling a corresponding number of claims. Upon entry of the above amendments, claims 17-39 will be pending. The specification has been

amended as required by the Examiner at page 2, ¶ 2 of the Office Action dated September 25, 2001 (Paper No. 9). Entry of the above amendments is requested.

Claim 16 has been canceled, and claim 39 added, to clarify the claimed method and to better point out the originality of the claimed invention. Specifically, the preamble of new claim 39 provides for a method for detecting and identifying DNA sequences involved in rearrangements of a target gene and for the use of an anchored PCR. The claimed method may be applied to one or several genes (i.e., at least one pair of primers is used).

The amendments are submitted to make it clear, if the same was needed, that, with the claimed method, rearrangements can be detected and the sequences involved in the rearrangements can be identified in the same experiment.

To the extent not obviated by the above amendments, the Section 112, second paragraph, rejection of claims 16-38 is traversed. Consideration of the following in this regard is requested (wherein the applicants have responded to the Examiner's individual objections by reference o the Examiner's subparagraphs).

A) The recitation of "a step of anchored PCR" has been amended.

B) and C) The claims have been amended to specify that one of the primers is a complementary anchored primer.

D) The objected-to phrase "all the gene rearrangements" has been amended for clarity, without prejudice, to advance prosecution.

E) The objected-to phrase "gene rearrangements" has been amended for clarity, without prejudice, to advance prosecution.

F) The objected-to phrase "any part of the genome adjacent to the target gene" has been amended for clarity, without prejudice, to advance prosecution.

G) The objected-to phrase " when present" has been deleted, without prejudice, to advance prosecution.

H) The reagents for carrying out the PCR and the detection have been specified.

I) The applicants respectfully submit claim 33 is clear and does not require amendment to include traditional "Markush" language. The same is not necessarily required and the Examiner has failed to indicated why one of ordinary skill in the art would not appreciate the meets and bounds of the subject matter of claim 33. Clarification is requested in this regard in the event the rejection of claim 33 is maintained.

J) The recitation of the objected-to phrase is submitted to be definite. Reconsideration and withdrawal of this objection of claim 33 is requested.

K) and L) The objected-to inclusion of the term "the" has to be deleted to obviate the rejection.

Withdrawal of the Section 112, second paragraph rejection is requested.

The Section 103 rejection of claims 16-38 over Corral et al in view of Liu et al is traversed. Reconsideration and withdrawal of the rejection are requested.

Corral teaches means for detecting chromosomal rearrangements, but does not disclose means for identifying the rearrangements.

Liu teaches the amplification and sequencing of insert end segments from clones.

Contrary to the Examiner's opinion, the ordinarily skilled artisan would not have combined Corral and Liu teachings as such a combination would have resulted in a method which would have been difficult to carry out and time consuming, since it comprises a PCR amplification, followed by a sequencing step.

The cited documents do not suggest that more effective methods of identification than amplifying and sequencing should be used for identifying DNA sequences involved in chromosomal rearrangements.

There is no suggestion or teaching in Corral or Liu to look for a method directly giving the identification results. It is submitted therefore that the claimed method is patentable over Corral and Liu as it provides, at once, in the same experiment, the detection and the identification of the DNA sequences involved in rearrangements of a target gene or of target genes (several types of rearrangements can be identified if several target genes are amplified). There is no teaching or suggestion in this respect in Corral or Liu.

Withdrawal of the Section 103 rejection is therefore requested.

In view of the above, the claims are submitted to be in condition for allowance and a Notice to that affect is requested.

Respectfully submitted,

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MARKED UP SPECIFICATION

Amend the specification as follows.

Page 21, delete the paragraph on line 16 and insert the following therefor:

--(SEQ ID NO [N°] 2, 44 nucleotides, Tm = 84°C).--

Page 21, delete the paragraph on line 26 and insert the following therefor:

--(SEQ ID NO [N°] 3, 32 nucleotides, Tm = 84°C), and--

Page 21, delete the paragraph on line 33 and insert the following therefor:

--(SEQ ID NO [N°] 4, 29 nucleotides, Tm = 86°C), and--

Page 22, delete the paragraph on line 33 and insert the following therefor:

--(SEQ ID NO [N°] 5, 35 nucleotides, Tm = 81°C).--

Page 23, delete the paragraph spanning lines 5-6 and insert the following therefor:

-- - ribozyme 1: CUCCAGCUGA UGAGUCCGUG AGGACGAAAC CUUUGG

(SEQ ID NO [N°] 6)--

Page 23, delete the paragraph spanning lines 8-9 and insert the following therefor:

-- - ribozyme 2: CUGGAAUCUG AUGAGUCCGU GAGGACGAAA UUUUCUUC

(SEQ ID NO [N°] 7)--

IN THE CLAIMS

Amend the claims as follows:

Cancel claim 16, without prejudice

17. (Amended) The method of claim [16] 39, wherein the primers consist of 25 to 40 nucleotides.

18. (Amended) The method of claim [16] 39, further comprising, labeling said PCR products, denaturing said labeled PCR products, and contacting the denatured labeled PCR products with a nucleotide sequence complementary to a fusion partner nucleotide sequence.

21. (Amended) The method of claim [16] 39, wherein one of the primers consists of a sequence containing a cassette of 40 to 60 nucleotides and 10 to 20 T nucleotides, and the second primer is a random repeat of nucleotides.

22. (Amended) The method of claim [16] 39, wherein said part of the genome adjacent to the target gene is a fusion partner.

23. (Amended) The method of claim 22, comprising:

a) subjecting the patient's genome DNA or RNA to the action of a compound capable of cleaving or specifically inhibiting the DNA or RNA of the target gene, the fusion of which is to be detected,

b) performing said [asymmetrical] PCR,

c) reacting the PCR products thus obtained with two probes specific for each target gene, one being upstream, and the other one being downstream, and with probes complementary to known fusion partners,

a positive detection on the upstream probe and a negative detection on the downstream probe, corresponding to a rearrangement of the target genes, and a

negative detection for the known partner genes corresponding to the absence of fusion with a known fusion partner, or alternatively,

d) reacting the PCR products with a plurality of probes bonded to a miniaturized support, and detecting hybridization of the probes with the PCR products, if any.

25. (Amended) The method of claim 24, comprising

a) the RT synthesis of a cDNA pool from the patient's RNA, using primers with a [consisting of a] cassette [with 30 to 35 nucleotides with a sequence of 6 or 9 random nucleotides],

b) a PCR amplification using a first primer located on the MLL exon 5, as specific sense primer, the 3' primer being [the same on each cycle and] complementary to the oligonucleotide cassette used in the RT step.

29. (Amended) The method of claim [16] 39, wherein said pathology is leukemia.

30. (Amended) The method of claim [16] 39, wherein said pathology concerns solid tumors.

32. (Amended) A kit for the [diagnostic] detection and identification method according to claim [16] 39, comprising primers specific for the target genes and reagents for carrying out the anchored PCR and [the] detection step[, and primers selected in the group consisting of primers specific for the target gene and random partners].

34. (Amended) A kit according to claim 32, further comprising [probes selected from the group comprising] probes complementary to the target [gene] genes and probes complementary to known fusion partners.